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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,797	05/16/2001	James L. Hartley	0942.285000G	2106

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EXAMINER	
SCHLAPKOHL, WALTER	
ART UNIT	**PAPER NUMBER**
1636	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/855,797	HARTLEY ET AL.	
	Examiner	Art Unit	
	Walter Schlapkohl	1636	waf

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *79-104* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *79-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the papers filed 4/3/2007 in which claims 52-59, 61-68 and 71-78 were cancelled and claims 79-104 were added. Claims 79-104 are pending and under examination in the instant Office action.

Claim Objections

Claims 91 and 104 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 91 and 104 do not further limit claims 79 and 92, respectively, because the claims simply *replace* the first linear nucleic acid molecule with a library of nucleic acid molecules.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 79 & 92, and therefore dependent claims 80-91 and 93-104 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. **This is a new rejection necessitated by Applicant's amendment filed 4/3/2007.**

Claims 79 and 92 recite *in vitro* methods for producing a product nucleic acid molecule comprising one or more *lox* or *att* sites, the methods comprising generating a first nucleic acid molecule and contacting the linear nucleic acid molecule with an "adapter" or a second nucleic acid molecule comprising one or more *lox* or *att* sites and a topoisomerase "under conditions sufficient to add one adapter to each terminus of the linear nucleic acid molecule, thereby producing the product nucleic acid molecule" (claim 79) or "under conditions sufficient to add one second linear nucleic acid molecule to each terminus of the first linear nucleic acid molecule, thereby producing the product nucleic acid molecule" (claim 92). Claims 79 and 92 are vague and indefinite in that the "conditions sufficient to add" the linear nucleic acid molecule or adapter to the terminus/termini of the first nucleic acid molecule are unclear. Does Applicant intend any conditions under which the

topoisomerase functions as a ligase and fuses the termini of each of the respective nucleic acid molecules to each other, or does Applicant intend, e.g., a method wherein a topoisomerase is added to a reaction mixture which increases the efficiency of a recombination reaction between *att* or *lox* sites present within a first nucleic acid and the second nucleic acid (or adapter) by first generating a linear nucleic acid (with the topoisomerase) and then ligating the topoisomerase-cleaved nucleic acids together either with a topoisomeerase or with a site-specific recombinase such as Cre?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered

therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

This is a new rejection necessitated by Applicant's amendment filed 4/3/2007.

Note: for purposes of this rejection only Examiner has interpreted the claims to be drawn to conditions wherein the first linear nucleic is added to the adapter and/or to the second nucleic acid molecule with the use of a topoisomerase.

Claims 79-85, 87-88, 90-98, 100-101 and 103-104 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boyd (*Nucleic Acids Research* **21**(4):817-821, 1993; of record) in view of Fox et al (US Patent No. 6,140,086).

Boyd teaches an *in vitro* method for high-speed cloning comprising producing one or more product nucleic acid molecules comprising two or more *lox* or *att* sites, the method comprising:

(a) generating a linear nucleic acid molecule; and

(b) contacting the linear nucleic acid molecule with (i) one or more "adapters" comprising one or more *lox* sites and (ii)

a DNA ligase, under conditions sufficient to add one "adapter" to each terminus of the linear nucleic acid molecule, thereby producing the product nucleic acid molecule (see entire document, especially page 818 and Figure 2). With regard to claims 80-81, 84, 93-94 and 97, Boyd teaches that blunt-ended fragments could be produced by PCR amplification or by cDNA synthesis (see page 817, column one and page 82, second paragraph). Regarding claims 82 and 95, on page 817 Boyd teaches the use of nucleic acids with *SalI* ends. Regarding claims 83 and 95, Boyd teaches that fragments were obtained from amplification of inter-Alu region of total genomic DNA from a hybrid cell line B2.13 (page 818). Regarding claims 87-88 and 100-101, Boyd teaches that the *lox* sites added to either end of the linear nucleic acid can be the same (i.e., the same sequence in the same orientation) or different (i.e., the same sequence in reverse orientation) (see, e.g., page 819, Figure 2). Regarding claims 85, 90, 98 and 103, Boyd teaches that the *lox* sites are from bacteriophage P1 (and therefore *lox*P sites) and that the *lox* sites have been engineered insofar as they have been constructed within a *SalI* cohesive ended duplex and mechanically synthesized (see page 817 last paragraph and the Abstract). With regard to claims 91 and 104, Boyd teaches that the method can be performed with a library of linear nucleic

acids, i.e. amplified segments of total genomic DNA (see paragraph bridging 1st and 2nd columns on page 818).

Boyd does not teach this procedure wherein topoisomerase is used as the DNA ligase to add the adapters comprising *lox* sites to each terminus of the linear nucleic acid molecule, thereby producing the product nucleic acid molecule.

Fox et al teach methods and compositions for high-effeciency, rapid cloning of nucleic acids, including methods for inserting amplified nucleic acids of interest into a vector (see entire document, especially columns 5-8). Fox et al teach that, like T4 DNA ligase, topoisomerase can be used to ligate amplified, synthesized or digested nucleic acid molecules (see entire document, especially column 11, lines 56-61; column 7, lines 41-45; and column 18, lines 17-25).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute *in vitro* recombination performed by topoisomerase as taught by Fox et al in the method of synthesizing one or more nucleic acid molecules as taught by Boyd because Fox et al teach that it is within the skill of the art to utilize T4 DNA ligases as well as topoisomerases to recombine DNA, especially to ligate an insert into a vector, and Boyd teaches that it is within the skill of the art to synthesize one or more linear nucleic acid molecules

to add to one or more "adapters" comprising one or more *lox* sites to each end of the linear nucleic acid in order to achieve rapid and efficient cloning of a nucleic acid of interest.

One of ordinary skill in the art would have been motivated to substitute the use of topoisomerase as taught by Fox et al in the method as taught by Boyd simply as a matter of designer's choice since both T4 DNA ligase and topoisomerase would serve the same purpose in Boyd's method of turbo cloning.

Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result when utilizing a topoisomerase instead of a T4 DNA ligase as taught by Fox et al in Boyd's method of attaching nucleic acids comprising one or more *lox* or *att* sites to each end of a first linear nucleic acid.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent applications to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at (800) 786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Joseph Woitach can be reached at (571) 272-0739.

Walter A. Schlapkohl, Ph.D.
Patent Examiner
Art Unit 1636

June 7, 2007

DAVID GUZO
PRIMARY EXAMINER